

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

| | | | | | |
|----------------------|---------------|--------------------|--|------------------------------|------------|
| Policy Number | NEU12182013RP | Approved By | UnitedHealthcare Medicare Reimbursement Policy Committee | Current Approval Date | 12/18/2013 |
|----------------------|---------------|--------------------|--|------------------------------|------------|

IMPORTANT NOTE ABOUT THIS REIMBURSEMENT POLICY

This policy is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

You are responsible for submission of accurate claims. This reimbursement policy is intended to ensure that you are reimbursed based on the code or codes that correctly describe the health care services provided. UnitedHealthcare reimbursement policies use Current Procedural Terminology (CPT®*), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT or other sources are for definitional purposes only and do not imply any right to reimbursement.

This reimbursement policy applies to all health care services billed on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450). Coding methodology, industry-standard reimbursement logic, regulatory requirements, benefits design and other factors are considered in developing reimbursement policy.

This information is intended to serve only as a general resource regarding UnitedHealthcare’s reimbursement policy for the services described and is not intended to address every aspect of a reimbursement situation. Accordingly, UnitedHealthcare may use reasonable discretion in interpreting and applying this policy to health care services provided in a particular case. Further, the policy does not address all issues related to reimbursement for health care services provided to UnitedHealthcare enrollees. Other factors affecting reimbursement may supplement, modify or, in some cases, supersede this policy. These factors may include, but are not limited to: legislative mandates, the physician or other provider contracts, and/or the enrollee’s benefit coverage documents. Finally, this policy may not be implemented exactly the same way on the different electronic claims processing systems used by UnitedHealthcare due to programming or other constraints; however, UnitedHealthcare strives to minimize these variations.

UnitedHealthcare may modify this reimbursement policy at any time by publishing a new version of the policy on this Website. However, the information presented in this policy is accurate and current as of the date of publication.

*CPT copyright 2010 (or such other date of publication of CPT) American Medical Association. All rights reserved. CPT is a registered trademark of the American Medical Association.

Proprietary information of UnitedHealthcare. Copyright 2014 United HealthCare Services, Inc.

Table of Contents

| | |
|---|----------|
| Application | 1 |
| Summary | 2 |
| Overview | 2 |
| Documentation Requirements | 7 |
| CPT/HCPCS Codes | 7 |
| References Included (but not limited to): | 8 |
| CMS Articles | 8 |
| CMS LCDs | 8 |
| CMS Benefit Policy Manual | 8 |
| CMS Claims Processing Manual | 8 |
| UnitedHealthcare Medicare & Retirement Reimbursement Policies | 8 |
| Others | 8 |
| History | 8 |

Application

This reimbursement policy applies to services reported using the Health Insurance Claim Form CMS-1500 or its electronic equivalent or its successor form, and services reported using facility claim form CMS-1450 or its electronic equivalent or its successor form. This policy applies to all products, all network and non-network physicians, and other health care professionals.

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing UnitedHealthcare. It is not enough to link the procedure code to a correct, payable ICD-9-CM diagnosis code. The diagnosis must be present for the procedure to be paid. Compliance with the provisions in this policy is subject to monitoring by pre-payment review and/or post-payment data analysis and subsequent medical review. The effective date of changes/additions/deletions to this policy is the committee meeting date unless otherwise indicated. CPT codes and descriptions are copyright 2010 American Medical Association (or such other date of publication of CPT). All rights reserved. CPT is a registered trademark of the American Medical Association. Applicable FARS/DFARS restrictions apply to Government use. Fee schedules, relative value units, conversion factors, and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Current Dental Terminology (CDT), including procedure codes, nomenclature, descriptors, and other data contained therein, is copyright by the American Dental Association, 2002, 2004. All rights reserved. CDT is a registered trademark of the American Dental Association. Applicable FARS/DFARS apply.

Summary

Overview

Colony Stimulating Factors (CSF) are hematopoietic growth factors, which act on progenitor cells capable of forming either single differentiated (lineage-specific) cell types, such as the neutrophilic granulocyte, or forming several differentiated cell types (i.e., non-lineage-specific). Whereas both filgrastim, and its longer-acting pegylated form, pegfilgrastim, act only on progenitor cells that are already committed to one pathway, thus increasing only the neutrophil (i.e., granulocyte) count, sargramostim promotes the formation of granulocyte, macrophage and mixed granulocyte-macrophage colonies.

- A. Human granulocyte colony-stimulating factors (Filgrastim and Pegfilgrastim) are drugs that are produced by recombinant DNA technology with the use of bacteria and a human G-CSF gene. G-CSF regulates the production of neutrophils (a WBC) within the bone marrow (where blood cells are manufactured naturally in the body). Neutrophils are an essential in the body's fight against infections.
- B. Granulocyte macrophage colony-stimulating factor (Sargramostim) is a recombinant human granulocyte-macrophage colony-stimulating factor produced by recombinant DNA technology in yeast. Granulocytes and macrophage cells (WBC's) are essential in the body's fight against infections.

G-CSF is classified as a recombinant hematopoietic stimulant. This is not a cancer chemotherapy agent. It is a class II hematopoietic growth factor which acts on progenitor cells capable of forming a single differentiated cell type, the neutrophilic granulocyte, and is thus lineage-specific. Because Filgrastim acts only on progenitor cells that are already committed to one pathway, it increases only the neutrophil (e.g., granulocyte) count.

Pegfilgrastim is approved by the Food and Drug Administration to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Indications for GM-CSF (J2820) and rG-CSF (J1440/J1441, J2505)

- For treatment of drug-induced neutropenia
- For treatment of severe, chronic neutropenia, including congenital, idiopathic, and cyclic
- To enhance neutrophil function in patients with myelodysplastic syndromes and history of infection
- To treat acquired immunodeficiency syndrome (AIDS) patients with neutropenia caused by the disease itself or infection with opportunistic organisms or antiretroviral agents
- For prolonging survival in patients who have undergone allogeneic or autologous Bone marrow transplant (BMT) in whom engraftment is delayed or has failed in the presence or absence of infection
- To enhance peripheral progenitor cell yield in autologous hematopoietic stem cell transplantation
For acceleration of myeloid recovery in patients undergoing allogeneic or autologous BMT following myeloablative chemotherapy for myeloid or nonmyeloid malignancies

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

- For acceleration of myeloid recovery in patients with non-Hodgkin's lymphomas, acute lymphoblastic leukemia and Hodgkin's disease undergoing autologous bone marrow transplant (BMT)
- For acceleration of myeloid recovery in patients who have undergone hematopoietic stem cell transplantation following myeloablative chemotherapy
- For treatment of diffuse large B cell Lymphoma

Indications for GM-CSF (J2820) and G-CSF (J1440/J1441)

- Acceleration of myeloid recovery in patients undergoing allogenic or autologous bone marrow transplantation following myeloablative chemotherapy for myeloid and non-myeloid malignancies.
- Severe symptomatic chronic neutropenia, including congenital neutropenias, cyclic neutropenias and idiopathic neutropenias
- Mobilization of peripheral stem cells when the transplant procedure itself is a covered benefit (See NCD 110.8.1).
- HIV as follows:
 - a. AIDS leukopenia in children;
 - b. Amelioration of leukopenia in AIDS patients on AZT;
 - c. Amelioration of leukopenia in AIDS patients with CMV chorioretinitis on Ganciclovir;
 - d. Treatment of HIV infection-associated neutropenia.
- Decreasing the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe febrile neutropenia. Patients experiencing an episode of febrile neutropenia are most likely to have subsequent episodes and are eligible for such prophylaxis.
- Enhancing neutrophil function in patients with myelodysplastic syndromes and a history of infection.
- Drug induced neutropenia in patients with a history of infection.
- Promoting myeloid engraftment following autologous or allogenic bone marrow transplantation or stem cell transplantation and in prolonging survival in patients who have undergone autologous or allogenic bone marrow transplants in whom engraftment is delayed or has failure in the presence or absence of infection.
- Patients at higher risk for chemotherapy-induced infectious complications, even though the data supporting such use are not conclusive. Such risk factors might include the following: pre-existing neutropenia due to disease, extensive prior chemotherapy, or previous irradiation to the pelvis or other areas containing large amounts of bone marrow; a history of recurrent febrile neutropenia while receiving earlier chemotherapy of similar or lesser dose-intensity; or conditions potentially enhancing the risk of serious infection, e.g., advanced physiologic age or frailty, poor performance status and more advanced cancer, decreased immune function, open wounds, or already-active tissue infections. (The possible risk factors in this paragraph are not meant to be all-inclusive.)
- Filgrastin: decreasing the duration of neutropenia after the completion of acute myelocytic leukemia (AML) induction or consolidation chemotherapy in adult patients.
- Sagramostim: decreasing the duration of neutropenia after the completion of acute myelocytic leukemia (AML) induction chemotherapy in older patients (55 years of age and older).

Indications for rG-CSF only (J1440/J1441, J2505)

- In adult and pediatric cancer patients receiving myelosuppressive chemotherapy
- Decreasing the duration of neutropenia and fever after the completion of AML induction or consolidation chemotherapy in adult patients

Indications for G-CSF only (J1440/J1441)

- To decrease the incidence of infection as manifested by febrile neutropenia, for patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
- Administration may be indicated for patients at high risk for chemotherapy-induced infectious complications. Such risk factors may include the following and should be documented in the patient record:

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

- a. Pre-existing neutropenia due to disease,
 - b. Extensive prior chemotherapy
 - c. Previous irradiation to the pelvis or other areas containing large amounts of bone marrow.
 - d. A history of recurrent febrile neutropenia while receiving earlier chemotherapy of similar or lesser dose-intensity
 - e. Conditions potentially enhancing the risk of serious infection.
- To reduce the duration of neutropenia and neutropenia related clinical sequelae (febrile neutropenia) for patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplant.
 - Peripheral Blood Progenitor Cell (PBPC) Collection-For the mobilization of hematopoietic progenitor cells into the peripheral blood for leukapheresis collection. Mobilization allows for collection of increased progenitor cell numbers capable of engraftment compared with collection by leukapheresis without mobilization or bone marrow harvest. After myeloablative chemotherapy, the transplantation of an increased number of progenitor cells can lead to more rapid engraftment, decreasing the need for supportive care.
 - Severe chronic neutropenia: chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g. fever, infections, and oropharyngeal ulcers) in symptomatic patients with congenital, cyclic or idiopathic neutropenia
 - Patients with Acute Myeloid Leukemia (AML) receiving induction or consolidation chemotherapy
 - Acquired immunodeficiency syndrome (AIDS) patients with neutropenia caused by the disease itself or by opportunistic infections
 - Medicare will consider G-CSF medically reasonable and necessary for the following off-label indications when it is not self/caregiver administered:
 - AIDS leukopenia in children.
 - Amelioration of leukopenia in AIDS patients on AZT.
 - Amelioration of leukopenia in AIDS patients with chorioretinitis on Ganciclovir.
 - Intermittent administration of G-CSF for a subset of patients with myelodysplastic syndromes (MDS) who have severe neutropenia and recurrent infections.
 - Severe aplastic anemia
 - Hairy cell leukemia
 - Myelodysplastic syndrome. It is not recommended for routine infection prophylaxis. Consider use if recurrent or resistant infections in neutropenic patients.
 - Drug induced or congenital agranulocytosis, alloimmune neonatal neutropenia.
 - Prophylactically used to decrease the incidence of infection, for patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of febrile neutropenia.
 - In cancer patients: Bone marrow transplant (BMT) - To reduce the severity of neutropenia in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by autologous BMT.
 - In Severe chronic neutropenia (SCN) patients: Congenital, cyclic, or idiopathic neutropenia - To reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with SCN.

Limitations for G-CSF only (J1440/J1441)

- A physician is not to bill Medicare for a supply of G-CSF given to the patient for self-administration at home. (See SAD RP)
- The following unlabeled uses of G-CSF have not been shown to be safe and effective and are non-covered by Medicare: aplastic anemia, hairy cell leukemia, myeloid malignancies (other than AML), drug-induced and congenital agranulocytosis, and alloimmune neonatal neutropenia.
- Therapeutic initiation of G-CSF does not add significantly to the antibiotic treatment outcome of established febrile neutropenia. Exceptions to this rule must be documented.
- There are inadequate data to support the use of G-CSF for patients with afebrile neutropenia.

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

- In general, for previously untreated patients receiving a chemotherapy regimen, primary administration of G-CSF is not considered medically necessary.
- G-CSF should not be given within 24 hours before or after a dose of a chemotherapeutic agent, as rapidly dividing myeloid cells are potentially sensitive to these agents.
- There is no evidence of benefit from the use of G-CSF to increase chemotherapy dose-intensity. G-CSF should not be used concurrently with radiation therapy.

Uses for which efficacy and safety have not been established:

- Administration of G-CSF in cancer patients in order to increase chemotherapy dose-intensity.
- Administration of G-CSF in patients with acute drug-induced myelosuppression is usually not medically necessary.
- Routine, continuous use of G-CSF in patients with myelodysplastic syndromes or Felty's syndrome without infections.
- Administration of G-CSF to patients undergoing chemotherapy and radiation concurrently.
- Administration of G-CSF in patients with chronic aplastic anemia. Growth factors, as single agents, have not been shown to be effective in severe aplastic anemia. Their use in combination with other agents such as cyclosporin and/or ALG is still investigational.

Indications for GM-CSF only (J2820)

1. To decrease the incidence of infection as manifested by febrile neutropenia, for patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. Acceleration of myeloid recovery in patients with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's disease undergoing autologous bone marrow transplantation (BMT). Indicate this by coding the BMT and NHL or ALL or Hodgkin's disease.
3. Bone Marrow Transplant failure or engraftment delay. For patients who have undergone allogeneic or autologous BMT in whom engraftment is delayed or has failed.
4. Induction chemotherapy in acute myelogenous leukemia (AML). The acceleration of neutrophil recovery following induction of chemotherapy in the treatment of patients over the age of 55-years old with acute myelogenous leukemia. Safety and efficacy has not been established in AML patients less than 55 years of age.
5. Mobilization and following transplantation of autologous peripheral blood progenitor cells. For mobilization of hematopoietic progenitor cells into peripheral blood collection by leukapheresis. After myeloablative chemotherapy, the transplantation of an increase number of progenitor cells can lead to rapid engraftment which may decrease the need for supportive care.
6. Myeloid reconstitution after allogeneic bone marrow transplant (BMT): For acceleration of myeloid recovery in patient's undergoing allogeneic BMT from human lymphocyte antigen (HLA) matched related donors. Safety and efficacy has been established in accelerating myeloid engraftment, reducing the incidence of bacteremia and other culture positive infections.
7. To increase WBC counts in patients with myelodysplastic syndromes.
8. Acquired Immunodeficiency Syndrome (AIDS) patients receiving zidovudine.
9. To decrease nadir of leukopenia secondary to myelosuppressive chemotherapy and decrease myelosuppression in preleukemic patients.
10. To correct neutropenia in aplastic anemia patients.
11. Drug induced or congenital agranulocytosis, alloimmune neonatal neutropenia.
12. Prophylactically used to decrease the incidence of infection, for patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of febrile neutropenia.
13. For the adjunct treatment of malignant melanoma following surgery for stage III or IV melanoma for those at high risk for recurrence.
14. To decrease the duration of neutropenia after the completion of acute myelocytic leukemia (AML)

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

induction chemotherapy in older adult patients.

15. For prolonging survival in patients who have undergone autologous or allogenic hematopoietic stem cell transplantation in whom engraftment is delayed or has failed, in the presence or absence of infection

Limitations for GM-CSF only (J2820)

- A physician is not to bill Medicare for a supply of GM-CSF given to the patient for self-administration at home. (See SAD RP)
- The following off-labeled uses of GM-CSF have not been shown to be safe and effective and are non-covered by Medicare: aplastic anemia, hairy cell leukemia, severe chronic neutropenia which includes congenital (Kostmann's syndrome), idiopathic and cyclic.
- Treatment of drug-induced neutropenia, except when associated with the use of antiretroviral agents is an off-labeled indication and non-covered by Medicare.
- There is no evidence that GM-CSF is an important benefit in patients with refractory or relapsed myeloid leukemia.
- Therapeutic initiation of GM-CSF does not add significantly to the antibiotic treatment outcome of established febrile neutropenia.
CSFs should not be routinely used as adjunct therapy for the treatment of uncomplicated fever and neutropenia. Uncomplicated fever and neutropenia are defined as follows:
 - Fever of < 10 days in duration, and
 - No evidence of pneumonia, cellulitis, abscess, sinusitis, hypotension, multi-organ dysfunction, or invasive fungal infection, and
 - No uncontrolled malignancies.
- There is inadequate data to support the use of GM-CSF for patients with afebrile neutropenia. GM-CSF is contraindicated in patients with excessive leukemic myeloid blasts in the bone marrow or peripheral blood (> 10%).
- In general, for previously untreated patients receiving a chemotherapy regimen, primary prophylactic administration of GM-CSF is not considered medically necessary.
- Due to the potential sensitivity of rapidly dividing hematopoietic cells, GM-CSF should not be administered simultaneously with cytotoxic chemotherapy or radiotherapy or within 24 hours preceding or following chemotherapy or radiotherapy.
- There is no evidence of benefit from the use of GM-CSF to increase chemotherapy dose-intensity.

Indications for Pegfilgrastim (J2505)

- Decreasing the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.
- Prophylactically used to decrease the incidence of infection, for patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of febrile neutropenia
- Patients at higher risk for chemotherapy-induced infectious complications, even though the data supporting such use are not conclusive. Such risk factors might include the following: pre-existing neutropenia due to disease, extensive prior chemotherapy, or previous irradiation to the pelvis or other areas containing large amounts of bone marrow; a history of recurrent febrile neutropenia while receiving earlier chemotherapy of similar or lesser dose-intensity; or conditions potentially enhancing the risk of serious infection, e.g., advanced physiologic age or frailty, poor performance status and more advanced cancer, decreased immune function, open wounds, or already-active tissue infections. (The possible risk factors in this paragraph are not meant to be all-inclusive.)

Limitations of Colony Stimulating Factors In General

Colony stimulating factors are not covered when:

- Self-administered

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

- Administered by a caregiver
- Administered in association with radiation therapy
- Routinely used for afebrile neutropenia

Dosing Guidelines

The package insert instructions for dosage and duration of treatment should not be exceeded.

The following is the recommended dosage and frequency when administering this drug:

- BMT - Recommended dose following BMT is 10 mcg/kg/day given as an IV infusion of 4 or 24 hours or SC. The first dose should be administered at least 24 hours after chemotherapy and at least 24 hours after bone marrow infusion. The dose should be based on the neutrophil response. When the absolute neutrophil count (ANC) is $>1000/\text{mm}^3$ for 3 consecutive days, reduce the G-CSF dosage to 5 mcg/kg/day. If the ANC remains $>1000/\text{mm}^3$ for 3 more consecutive days, discontinue use.
- PBPC - Recommended dose is 10 mcg/kg/day SC. G-CSF should be given for at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis.
- Myelosuppressive chemotherapy - Recommended starting dose is 5 mcg/kg/day SC or short IV infusion (15-30 minutes), or by continuous infusion. Doses may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to duration and severity of the ANC nadir. Administer no earlier than 24 hours after cytotoxic chemotherapy and not in the 24 hours before administration of chemotherapy. The drug should be discontinued when the absolute neutrophil count (ANC) reaches $10,000/\text{mm}^3$ and/or the patient becomes afebrile, or the patient has received the drug for a maximum of 14 days per treatment regimen.
- AML - Recommended starting dose is 5mcg/kg/day SC until: ANC 1,000 cells/ mm^3 for 3 days or ANC $>10,000$ cells/ mm^3 for 1 day or for a maximum of 35 days.
- SCN - Starting dose for congenital neutropenia is 6 mcg/kg twice daily SC every day. Idiopathic or cyclic neutropenia starting dose is 5 mcg/kg as a single injection SC every day. Chronic daily administration is required to maintain clinical benefit. Individually adjust the dose based on the patient's clinical course, as well as the ANC. Reduce the dose if the ANC is persistently $>10,0000/\text{mm}^3$. The guidelines recommended for adults are generally applicable to the pediatric age group. Providers should make certain that when billing J2505 they show the correct number of multiples of 6 MG not the number of MGs.

Documentation Requirements

Medical record documentation maintained by the physician must clearly indicate:

- The patient's current absolute neutrophil count (ANC);
- The patient's weight in kilograms;
- The administration and dosage of the GM-CSF;
- The actual indication for which the drug was given and accompanying symptomology (e.g., fever); and
- The patient's response to the treatment.

This information is usually found in the history and physical or the office/progress notes. The ANC may be reported in the patient's laboratory report.

CPT/HCPCS Codes

| Code | Description |
|-------|--|
| J1440 | Injection, filgrastim (G-CSF), 300 mcg |
| J1441 | Injection, filgrastim (G-CSF), 480 mcg |
| J2505 | Injection, pegfilgrastim, 6 mg |
| J2820 | Injection, sargramostim (GM-CSF), 50 mcg |

Neupogen (Filgrastim)/Neulasta (Pegfilgrastim)

References Included (but not limited to):

CMS Local Coverage Articles

Numerous Articles

CMS LCDs

Numerous LCDs

CMS Benefit Policy Manual

Chapter 15 – Covered Medical and Other Health Services: §50

CMS Claims Processing Manual

Chapter 17 - Drugs and Biologicals

UnitedHealthcare Medicare & Retirement Reimbursement Policies

Medically Unlikely Edits

NCD 110.8.1 Stem Cell Transplantation

Self-Administered Drug

Others

FIRST COAST SERVICE OPTIONS LOCAL COVERAGE DETERMINATION CODING GUIDELINES attachment to L28967 (“Coding Guidelines” as stated above in the body of the policy for J2505)

History

| Date | Revisions |
|------------|--|
| 12/18/2013 | <ul style="list-style-type: none"> • New policy created to address coverage guidelines of Neupogen (Filgrastim)/Neulasta (Pegfilgrastim) • Presented to MRPC for approval. |